Individual Safety Report

3574775-8-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

McNeil Consumer Healthcare

McNeil Consumer Healthcare
Fort Washington, PA 19034-2299

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Approved by FDA on 11/15/93

Mfr report #

UF/Distr report #

FDA use only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
unknown In confidence	47 yrs or Date of birth:	( )female (X)male	unk lbs or kgs

B. Adverse event or product problem

1. X Adverse event and/or Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

( ) death (mo/day/yr)
( ) life-threatening
(X) hospitalization - initial or prolonged
( ) disability
( ) congenital anomaly
(X) required intervention to prevent permanent impairment/damage
(X) other: recovered

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
unknown	09/13/00

5. Describe event or problem

Abstract #161 from the 2000 North American Congress of Clinical Toxicology Annual Meeting of severe APAP hepatic (AGGRAVATED LIVER DAMAGE) & renal toxicity (KIDNEY FUNCTION ABNORMAL) following post operative therapeutic doses. According to abstract, a 47 yo male presented w/ CHF. MI was R/O, but the pt had hepatic injury (ALT=94 IU/L, LDH=1611 IU/L). SH included 6-8 beers daily & smoking. On day 4, CABPG was performed. Pt was not fed, but was started on iron sulfate 325 mg tid. Post-op meds included propoxyphene 100 mg/APAP 650 mg, APAP 325 mg/oxycodone 5 mg & APAP 325 mg/codeine 30 mg for pain & APAP 650 mg prn fever. Daily post-op APAP was 2.6g, 3.9g, 3.9g, 3.9g & 1.3g on postop day 5. Pt rec'd total of 15.6g. On post-op day 5, HYPOTENSION & disorientation developed. ALT/AST were 2613U/L & 4838U/L. LACTIC ACIDOSIS, HYPOGLYCEMIA, PANCREATITIS, renal insufficiency, & THROMBOCYTOPENIA followed. APAP level 8 hrs after the last dose was 15mcg/mL. All cultures were (-). Liver biopsy showed centrilobular necrosis (See Sect B7)

6. Relevant tests/laboratory data, including dates

initial: ALT=94 IU/L, LDH=1611 U/L; Post-op day 5: ALT=2613, AST=4838; APAP level 8 hrs after last dose=15 mcg/mL; all cultures were (-); liver biopsy: centrilobular necrosis

SEP 1 8 2000

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

preceding hepatic injury, 6-8 beers/day, smoking

(Sect B5 cont): (LIVER NECROSIS). Pt was tx'd w/ NAC for 17 doses. Pt reportedly recovered with aggressive supportive care.

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 unspecified acetaminophen product
#2 propoxyphene 100 mg/APAP 650 mg (See Sect C1)

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 650 mg, prn, po	#1 unknown dates; 5 days
#2 unknown dose, po	#2 unknown dates; 5 days

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 fever	#1 (X) Yes ( ) No ( ) N/A
#2 pain	#2 (X) Yes ( ) No ( ) N/A

6. Lot # (if known)	7. Exp. date (if known)	8. Event reappeared after reintroduction
#1 Unknown	#1 Unknown	#1 ( ) Yes ( ) No (X) N/A
#2 unknown	#2 unknown	#2 ( ) Yes ( ) No (X) N/A

9. NDC # - for product problems only (if known)

- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

unknown

(Sect C1 cont) #3 APAP 325 mg/oxycodone 5 mg, 5 days, for pain #4 APAP 325 mg/codeine 30 mg, 5 days, for pain

G. All manufacturers

1. Contact office - name/address (& mfr'g site for devices)

McNeil Consumer Healthcare
Medical Affairs
7050 Camp Hill Road
Ft. Washington, PA 19034

CENTER FOR DRUG EVALUATION AND RESEARCH RECEIVED SEP 2 0 2000

2. Phone number: 215-273-7303

3. Report source (check all that apply)
( ) foreign
( ) study
(X) literature
( ) consumer
(X) health professional
( ) user facility
( ) company representative
( ) distributor
( ) other:

4. Date received by manufacturer (mo/day/yr): 09/11/00

5. (A) NDA # 19-872
IND #
PLA #
pre-1938 ( ) Yes
OTC product (X) Yes

6. If IND, protocol #

7. Type of report (check all that apply)
( ) 5-day (X) 15-day
( ) 10-day ( ) periodic
(X) Initial ( ) follow-up #

8. Adverse event term(s)

LIVER DAMAGE AG
KIDNEY FUNC ABN
HYPOTENSION
ACIDOSIS LACTIC
HYPOGLYCEMIA
PANCREATITIS
THROMBOCYTOPENI
NECROSIS LIVER

9. Mfr. report number: 1428997A

E. Initial reporter

1. Name, address & phone #

[redacted]

DSS SEP 2 0 2000

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
(X) Yes ( ) No		( ) Yes ( ) No (X) Unk

FDA
Facsimile Form 3500A

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

160 SURVIVAL AFTER MASSIVE INGESTION OF ACETAMINOPHEN PRESENTING AS COMA AND METABOLIC ACIDOSIS.

Rusyniak D, Dribben W, Furbee B, Kirk M. *Indiana Poison Center, Indiana University School of Medicine, Clarian Health Partners, Indianapolis, IN*

Objective: We present an unusual clinical scenario associated with massive acetaminophen overdose that through aggressive supportive care resulted in a good outcome despite a complicated clinical course. Case Report: A previously healthy 26-year-old female presented 12 hours after ingesting approximately 125 grams of Extra-Strength Tylenol® comatose with a GCS of 3. Vital signs included temperature 35.6°C, SBP 60 mmHg, and HR 130/min. She was intubated, resuscitated with IV fluids and started on pressors. Initial laboratory data revealed marked metabolic acidosis (pH 6.7, bicarbonate 5 mmol/L), renal insufficiency (creatinine 1.8 mg/dL), mild hepatotoxicity (AST 121 U/L, total bilirubin 0.7 mg/dL), and mild coagulopathy (INR 1.38, platelets 80,000/mm^3). A 12-hour acetaminophen level was 1,148 mcg/mL followed by an 18 hour level of 1328 mcg/mL. Workup for other causes of metabolic acidosis (salicylates, iron, toxic alcohols) was negative. Despite treatment with IV NAC, the patient developed fulminant hepatic failure and underwent a 12 week hospital course including: 3 weeks of ventilatory support, prolonged hypotension (10 days of norepinephrine, max 68 mcg/kg/min), CVVH for renal failure, episodes of complete heart block, pancreatitis with pseudocyst, sepsis and pneumonia, ARDS, upper GI bleed, tracheo-esophageal fistula, pleural hematoma, pancyctopenia (treated with 27 units of PRBCs and 17 units of platelets), and coagulopathy requiring 20 units of FFP. She eventually recovered and was discharged home with a normal neurological outcome and normal hepatic function. Conclusions: Massive ingestions of acetaminophen can present as metabolic acidosis and coma before the onset of hepatic failure. Despite fulminant hepatic failure and criteria suggesting poor prognosis, patients can survive with aggressive supportive care and without liver transplantation.

161 SEVERE ACETAMINOPHEN HEPATIC AND RENAL TOXICITY FOLLOWING POSTOPERATIVE THERAPEUTIC DOSES.

Burkhart KK, Donovan JW. *The Pennsylvania State University, Hershey, PA*

Background: Acetaminophen (APAP) is used to help control pain postop. We describe a patient who had multiple APAP orders with the potential to receive excessive in-hospital APAP. Our patient received ≤3.9 g/d (total 15.6 g) and developed severe hepatic and renal toxicity. Case Report: A 47-year-old male presented with CHF. A MI was ruled out, but there was hepatic injury, ALT 94 U/L, and LDH 1611 U/L. SH included 6–8 beers/d and smoking. On day 4, CABPG was performed. The patient was not fed, but was started on iron sulfate 325 mg TID. On postop day 5 hypotension and disorientation developed. ALT/AST were 2613 and 4838 U/L. Lactic acidosis, hypoglycemia, pancreatitis, renal insufficiency, and thrombocytopenia followed. Postop APAP orders included propoxyphene 100 mg/APAP 650 mg, APAP 325 mg/oxycodone 5mg, and APAP 325 mg/codeine 30 mg for pain, and APAP 650 mg pm fever. Daily postop APAP was 2.6 g, 3.9 g, 3.9 g, 3.9 g, and 1.3 g on postop day 5. An APAP level 8 hours after the last dose was 15 mcg/mL. All cultures returned negative, while a liver biopsy showed centrilobular necrosis. *N*-acetylcysteine was given for 17 doses. With aggressive supportive care this patient recovered. Conclusions: This case is a rare report where therapeutic APAP doses produced severe toxicity. This patient had risk factors, preceding hepatic injury, postop wound healing and fasting, heavy alcohol consumer, and the iron. Hospitals must develop protocols that prevent patients from receiving ≥4 g/d of APAP. Our pharmacy instituted the following changes. Warning flags are in the computer to alert pharmacists to check doses. No more than 3 pm doses are sent to patient floors. Finally, labels have been placed on all APAP products from the automated dispensing equipment that warn nurses to check the patient's total APAP dosing.

162 HEMOLYSIS FOLLOWING ACETAMINOPHEN OVERDOSE IN A PATIENT WITH GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY.

Ruha AM, Selden B, Brooks D. *Good Samaritan Regional Medical Center, Phoenix, AZ*

Background: Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency hemolyze when oxidant stress depletes reduced glutathione in erythrocytes. Therapeutic doses of many drugs precipitate hemolytic episodes in such patients, however, acetaminophen (APAP) is not considered one of them. We describe acute hemolysis following a large ingestion of (APAP) in a patient with unrecognized G6PD deficiency. Case Report: A 16-year-old African-American teenager, with previously undiagnosed G6PD deficiency, ingested an unknown amount of APAP, fluvoxamine, and clomipramine in a suicide attempt. A 6 hour. APAP level was 680 mg/L. He received intravenous *N*-acetylcysteine